MEDICATION ADHERENCE AND DISCONTINUATION IN PATIENTS WITH SCHIZOPHRENIA TREATED WITH ARIPIPRAZOLE ONCE-MONTHLY LONG-ACTING INJECTABLE VERSUS THOSE TREATED WITH ORAL ANTIPSYCHOTICS

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Background

- Schizophrenia (SCZ) is a chronic psychiatric disorder that affects approximately 2.8 million adults in the United States.[1]
- Medication non-adherence is associated with greater risks of relapse of symptoms and repeated hospitalizations.[2,3]
- Long-acting injectable antipsychotics (LAIs) have been shown to improve medication adherence and discontinuation risk when compared to oral antipsychotic monotherapy.[4]
  - Previous studies have only included small sample sizes of aripiprazole once-monthly LAI (AOM 400) users[5]
- This study aimed to compare medication adherence and discontinuation in patients with SCZ treated with AOM 400 to those who changed to a different oral antipsychotic.

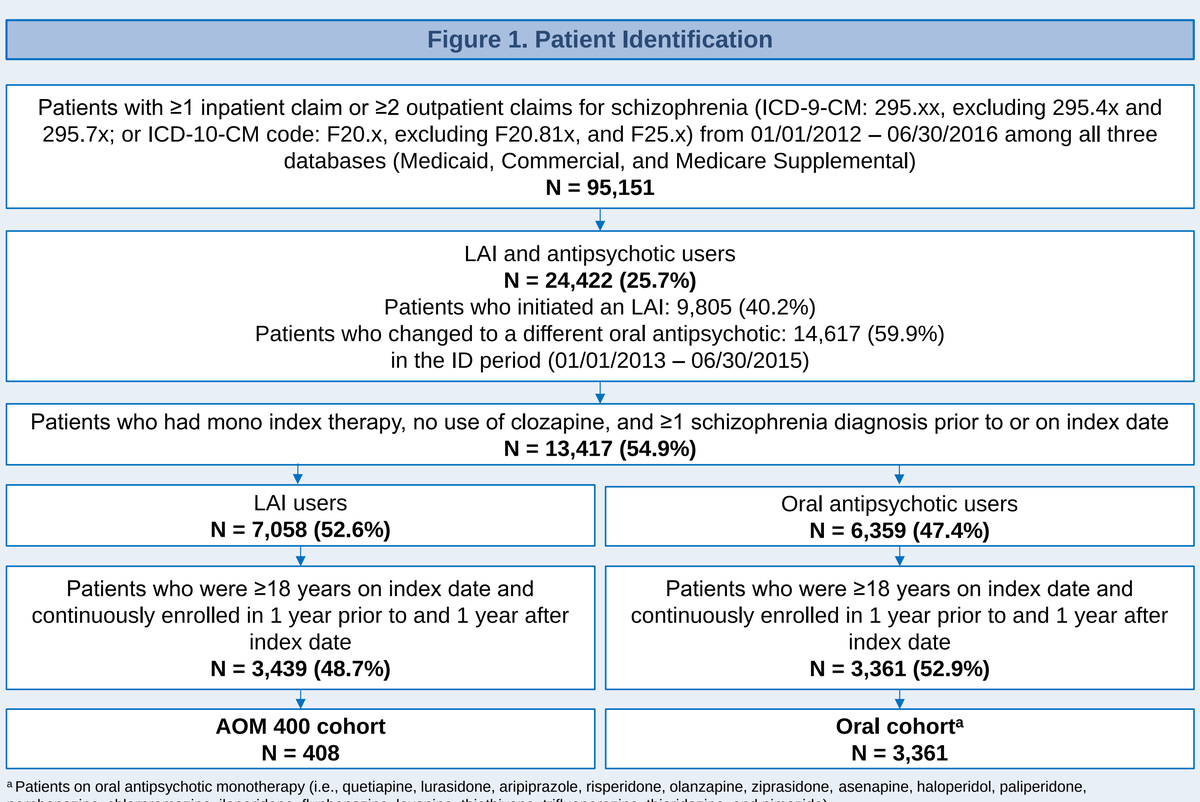
Methods

- Retrospective cohort study using the Truven Health MarketScan® Medicaid, Commercial, and Medicare Supplemental Databases
- Patient identification:
  - ≥1 inpatient or ≥2 outpatient claims for existing or newly diagnosed SCZ (ICD-9-CM: 295.xx, excluding 295.4x and 295.7x; or ICD-10-CM: F20.x, excluding F20.81x) between 01/01/2012 and 06/30/2016
  - AOM 400 cohort
    - Initiated AOM 400 during the ID period (01/01/2013 to 06/30/2015)
    - Index date: first date of starting AOM 400
    - No AOM 400 use 1 year prior to the index date (use of a different LAI was allowed)
  - Oral cohort
    - SCZ patients who changed to a different oral antipsychotic monotherapy
    - Index date: first date of starting new oral antipsychotic
  - Additional inclusion criteria
    - Schizophrenia diagnosis before index date
    - 1-year pre-index (baseline) continuous enrollment
    - ≥1-year post-index follow-up until disenrollment or study end
  - Exclusion criteria
    - ≤17 years old on index date
    - Use of clozapine during the study period, as clozapine is indicated for severely ill patients with SCZ who fail to respond adequately to standard antipsychotic treatments
    - Patients who were Medicare and Medicaid dual eligible, without pharmacy coverage, without mental health coverage information, or had capitated plans, as data may be incomplete
  - Patients followed for variable period until disenrollment or study end
- Medication adherence reported as proportion of days covered (PDC) during 1-year follow-up
  - PDC = number of days when index medication was available / 365 days
- Discontinuation defined as switch of index treatment or gap of ≥60 days
- Statistical analysis:
  - A general linear regression model used to estimate medication adherence
  - A Cox regression model used to estimate time to discontinuation and risk of discontinuation
  - All models adjusted for patient demographic and clinical characteristics, baseline psychiatric comorbidity, baseline psychiatric and somatic medication use, and baseline hospitalization

Results

- We identified 408 (10.8%) AOM 400 patients and 3,361 (89.2%) oral antipsychotic patients (Figure 1; Table 1).
- AOM 400 patients had better medication adherence (adjusted mean PDC: 57.0% vs. 47.6%, p<0.001) than the oral cohort during the 1-year follow-up period.
  - 63.0% of AOM 400 patients were partially (PDC 40%-79%) to fully adherent (PDC ≥80%) vs. 51.1% of oral antipsychotic patients (p<0.001) (Figure 2).
  - Adjusted mean PDC for AOM 400 vs. oral antipsychotics: 57.0% vs. 47.6%, p<.001
- AOM 400 patients also had a lower medication discontinuation rate than the oral cohort during the 1-year follow-up and a longer time to discontinuation in the entire follow-up period.
  - The discontinuation rate was 75.2% for AOM 400 vs. 85.0% for the oral cohort (p<.001) (Figure 3).
  - Median time to discontinuation was 193 days for AOM 400 vs. 89 days for oral antipsychotics (p<0.001) during the entire follow-up period (Figure 3).
  - In the Cox model, the oral cohort was more likely to discontinue their index treatment than AOM 400 patients (hazard ratio: 1.45; p<0.001) (Table 2).

Figure 1. Patient Identification



[a] Patients on oral antipsychotic monotherapy (i.e., quetiapine, lurasidone, aripiprazole, risperidone, olanzapine, ziprasidone, asenapine, haloperidol, paliperidone, perphenazine, chlorpromazine, iloperidone, fluphenazine, loxapine, thiothixene, trifluoperazine, thioridazine, and pimozide)

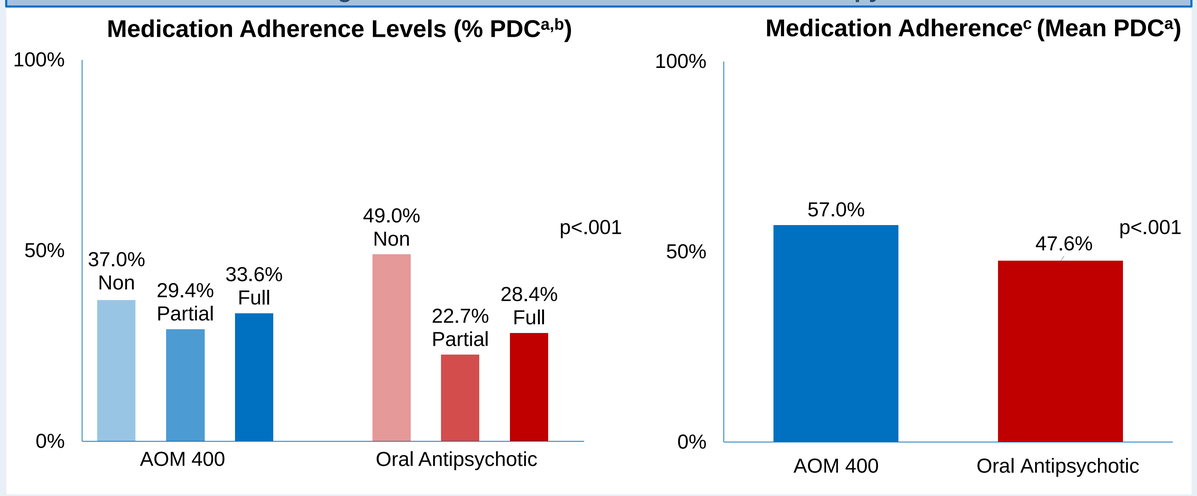
Results (continued)

Table 1. Demographics and clinical characteristics

	AOM 400 N = 408; 10.8%	Oral Antipsychotics[a] N = 3,361; 89.2%	All N = 3,769	P Value
Age in years, mean (SD)	37.3 (13.4)	43.6 (15.9)	42.9 (15.8)	<.001
Female, n (%)	172 (42.2)	1,751 (52.1)	1,923 (51.0)	<.001
Race, n (%)				<.001
White	112 (27.5)	844 (25.1)	956 (25.4)	
African American	182 (44.6)	1,043 (31.0)	1,225 (32.5)	
Other	40 (9.8)	431 (12.8)	471 (12.5)	
Unknown (Commercial/Medicare supplemental)	74 (18.1)	1,043 (31.0)	1,117 (29.6)	
Insurance Type, n (%)				<.001
Medicaid	334 (81.9)	2,318 (69.0)	2,652 (70.4)	
Commercial	66 (16.2)	804 (23.9)	870 (23.1)	
Medicare supplemental	8 (2.0)	239 (7.1)	247 (6.6)	
Comorbidities				
Charlson comorbidity index, mean (SD)	1.0 (1.6)	1.5 (2.1)	1.4 (2.0)	<.001
No. chronic conditions, mean (SD)	3.6 (2.3)	4.3 (2.4)	4.2 (2.4)	<.001
Psychiatric comorbidities[b], n (%)	282 (69.1)	2,578 (76.7)	2,860 (75.9)	<.001
Somatic comorbidities[c], n (%)	230 (56.4)	2,086 (62.1)	2,316 (61.4)	0.026
Baseline[d] medication and healthcare service use				
Any use of psychiatric medications[e], n (%)	308 (75.5)	2,750 (81.8)	3,058 (81.1)	0.002
Somatic medications[f], n (%)	185 (45.3)	1,751 (52.1)	1,936 (51.4)	0.010
Any hospitalization, n (%)	182 (44.6)	1,832 (54.5)	2,014 (53.4)	<.001

[a] Patients with oral antipsychotic (i.e. quetiapine, risperidone, olanzapine, lurasidone, aripiprazole, ziprasidone, haloperidol, paliperidone, asenapine, perphenazine, fluphenazine, iloperidone, chlorpromazine, loxapine, thiothixene, trifluoperazine, pimozide, and thiordazine)
[b] Bipolar disorders, major depressant disorders, anxiety, personality disorder, substance abuse disorders
[c] Obesity, diabetes mellitus Type 2, hyperlipidemia, hypertension
[d] One year prior to the index date
[e] Antidepressant, anti-anxiety medications, sedatives or hypnotics, mood stabilizer
[f] Antidiabetic medications, lipid-lowering medications, antihypertensive medications

Figure 2. Medication Adherence to Index Therapy



[a] PDC: Proportion of days covered, number of days during year when medication was available/365. [b] Non-adherence: PDC<40%; partial: 40%≤PDC<80%; full: PDC≥80%. [c] General linear regression model; adjusted by age group, gender, insurance type, Charlson comorbidity, no. of chronic conditions, baseline psychiatric comorbidity, baseline psychiatric medication use, baseline somatic medication use, and baseline hospitalization.

Figure 3. Discontinuation of Index Therapy

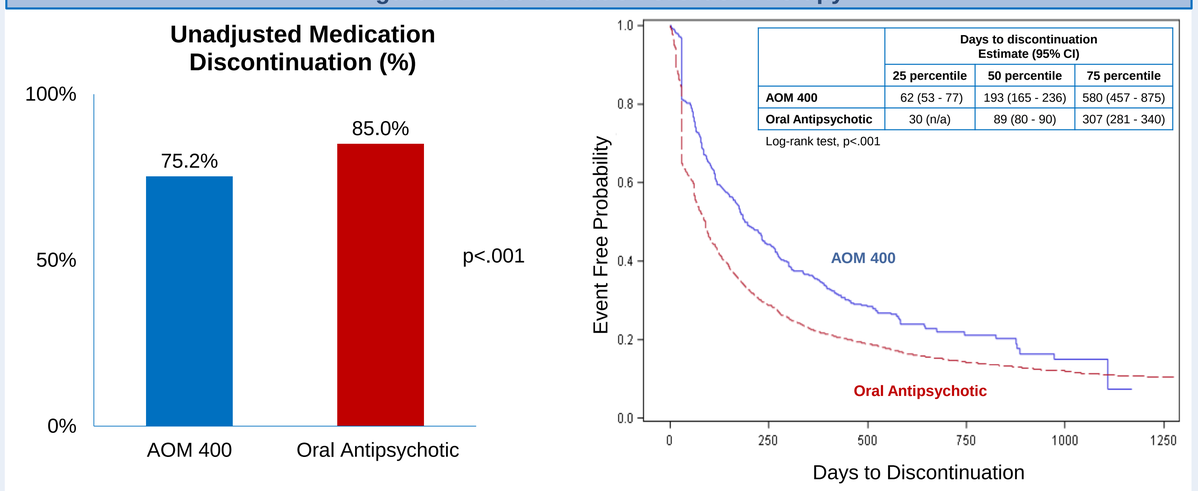


Table 2. Adjusted[a] Risk of Discontinuation of Index Treatment in Follow-up Period[b]

	HR (95% CI)	P Value
Oral monotherapy (Ref: AOM 400)	1.45 (1.29 – 1.64)	<.001

[a] Adjusted by age group, gender, insurance type, Charlson comorbidity, no. of chronic conditions, baseline psychiatric comorbidity, baseline psychiatric medication use, baseline somatic medication use, and baseline inpatient hospitalization.
[b] Cox regression model.

Discussion

- This real-world study suggests that patients with schizophrenia initiating AOM 400 had better medication adherence and lower discontinuation risk than patients who changed to a different oral antipsychotic.
- These results add to the growing literature demonstrating the advantages of LAIs over oral antipsychotics by examining the benefits of a specific LAI, AOM 400.
- Limitations of the study include that claims are meant for reimbursement, not research purposes, so misclassification is possible, and claims for a medication indicate that a prescription was filled and not that it was actually taken as prescribed.

References

1. Cloutier M, et al. J Clin Psychiatry. 2016;77(6):764-71. doi: 10.4088/JCP.15m10278.
2. Weiden PJ, et al. Psychiatr Serv. 2004;55(8):886-91. doi: 10.1176/appi.ps.55.8.886.
3. Lang K, et al. Psychiatr Serv. 2010;61(12):1239-47. doi: 10.1176/ps.2010.61.12.1239.
4. Greene M, et al. J Med Econ. 2018;21(2):127-34. doi: 10.1080/13696998.2017.1379412.
5. Pilon D, et al. BMC Psychiatry. 2017;17(1):207. doi: 10.1186/s12888-017-1358-3.

Disclosures: Greene and Pulaski are employees of Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ. Chang, Yan, and Broder are employees of Partnership for Health Analytic Research, LLC, Beverly Hills, CA. Hartry is an employee of Lundbeck, Deerfield, IL. Funding for the study and this poster was received from Otsuka Pharmaceutical Development and Commercialization, Inc. and Lundbeck.

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